Cutaneous lymphoid hyperplasia arising in pre-existing morphea plaques treated with methotrexate

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INTRODUCTION

Morphea, also known as *localized scleroderma*, is characterized clinically by indurated skin and fibrosis of the dermis or subcutaneous tissue. Its etiology is unknown.[1] Based on clinical presentation, morphea is classified into plaque, generalized, bullous, linear, and deep morphea types. Several types of morphea may be present in the same patient.[2] Cutaneous lymphoid hyperplasia (CLH) is defined as cutaneous B-cell infiltrates that resemble B-cell lymphoma clinically and histologically.[3] Herein we report a case of CLH arising in pre-existing morphea plaques treated with methotrexate.

Abbreviations used:

CLH: cutaneous lymphoid hyperplasia
CTD: connective tissue diseases

CASE REPORT

A 69-year old white woman presented with multiple indurated skin lesions over the trunk for 6 months. Medical history was unremarkable; notably negative for Raynaud phenomenon or systemic symptoms. Physical examination found multiple large indurated symmetrical plaques, with violet-colored borders, on the chest, flanks, and back (Fig 1).

Laboratory investigations were all within the normal range, including autoantibody profile (antinuclear antibodies, anti−ds-DNA, anti−scl-70, anticentromere, antihistone, antiphospholipid antibodies, rheumatoid factor, antithyroid antibodies). A skin biopsy found dermal thickening by dense collagen bundles with focal and moderate interstitial lymphocytic infiltrate. This histologic aspect was compatible with morphea, and the diagnosis of generalized morphea was established.

The lesions were deemed active because of their increasing numbers and peripheral "lilac rings." The patient was treated with 30 sessions of psoralen ultraviolet A (PUVA) photochemotherapy without improvement. During this time, the patient had multiple painful nodules over morphea plaques. There were no clinical signs of infection, and the patient denied trauma, scratching, or any new medications. Clinical examination found multiple infiltrated erythematous nodules over the chest and the scapular regions (Fig 2). There were no palpable lymph nodes or enlarged liver or spleen.

A skin biopsy of the nodular lesion showed thickening and hyalinization of the reticular dermis, consistent with previously diagnosed underlying morphea, associated with dermal and subdermal dense lymphocytic infiltrates with the formation of several lymphoid follicles with germinal centers, containing tingible body macrophages. The biopsy also found a diffuse infiltrate of plasma cells and eosinophils (Figs 3, *A* and 4, *A*). There was no cytonuclear atypia.

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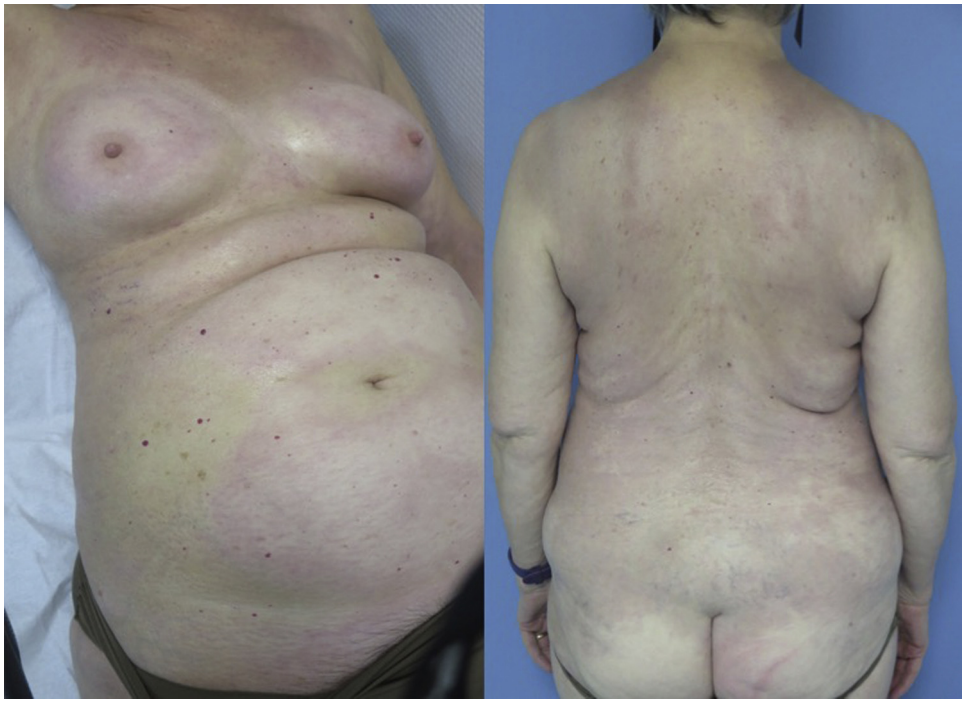

Fig 1. Multiple large indurated symmetrical plaques, with violet-colored borders, on the chest, flanks, and back.

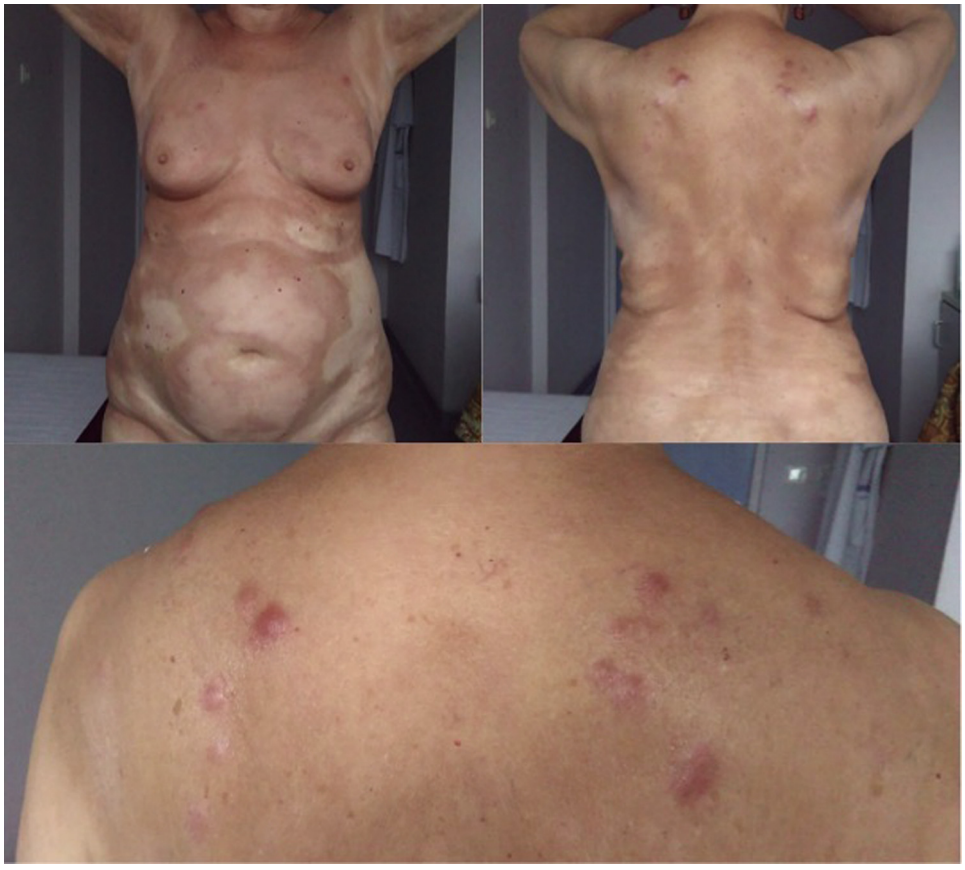

Fig 2. Multiple infiltrated erythematous nodules over the chest and the scapular regions.

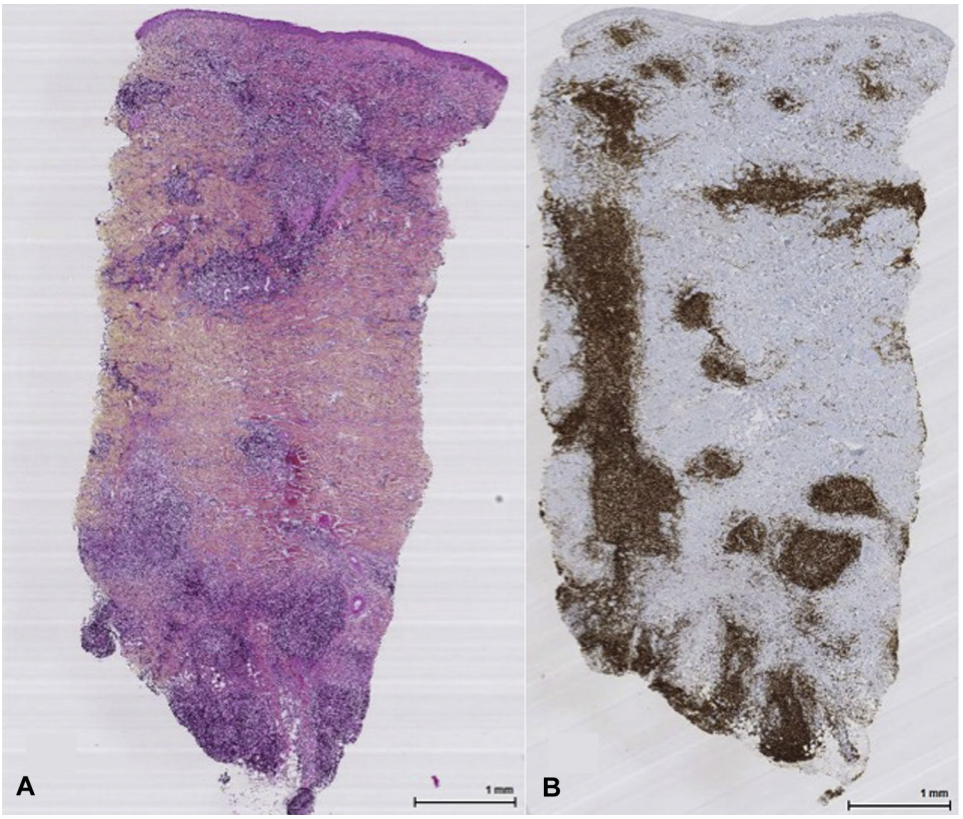

Fig 3. **A**, Skin biopsy shows thickening and hyalinization of the reticular dermis associated with dermal and subdermal dense lymphocytic infiltrates with the formation of several lymphoid follicles/germinal centers. **B**, Immunohistochemistry shows most of the infiltrate represented by $CD20^{+}$ B cells. ×10. (**A**, Hematoxylin phloxine saffron stain; original magnifications: **A** and **B**, ×10.)

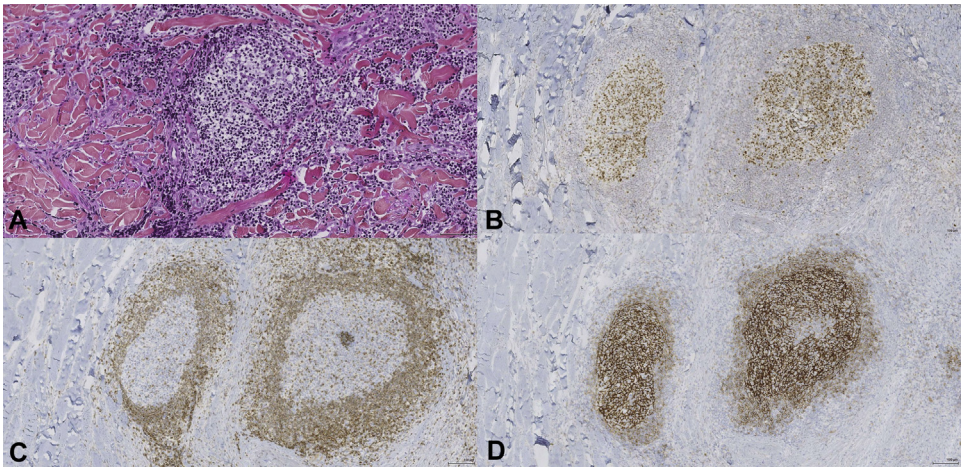

Fig 4. **A**, Lymphoid follicle with germinal center. Note some histiocytes and some eosinophils in the peripheral. **B**, Bcl-6 immunoreactivity inside germinal centers. **C**, Bcl-2 expression is absent inside some germinal centers. **D**, $CD23^{+}$ follicular dendritic cell network was regularly structured. (**A**, Hematoxylin phloxine saffron stain; **B-D**, immunohistochemistry; original magnifications: **A**, ×170; **B-D**, ×100.)

Immunohistochemistry study found most of the infiltrate represented by $CD20^+$ B cells (Fig 3, *B*). The germinal center cells expressed Bcl-6, CD10 and some small cells expressed Bcl-2 (Fig 4, *B* and *C*). Ki-67 was elevated and confined in the germinal centers. $CD23^+$ follicular dendritic cell network was regularly structured (Fig 4, *D*). Plasma cells CD138 were seen in significant amounts. The expression of immunoglobulin light chains κ and λ by plasma cells were polytypic (in situ hybridization). The diagnosis of CLH was established.

Computed tomography of the chest and abdomen ruled out lymph node enlargement or hepatosplenomegaly. The complete blood counts and peripheral lymphocyte immunophenotyping by flow cytometry were unremarkable. Lyme IgM/IgG antibodies were negative.

Doxycycline, 200 mg/d for 3 weeks was prescribed with no effect. Methotrexate, 25 mg/wk, was therefore prescribed. Six months later, morphea plaques were improved and less indurated with apparent regression of the nodules.

DISCUSSION

Cutaneous pseudolymphoma is defined as localized, reactive, polyclonal benign lymphoproliferative process composed of either B cells or T cells, which may resemble clinically and histologically malignant lymphomas. CLH is a cutaneous B-cell pseudolymphoma that presents with asymptomatic, indolent, nodular lesions, usually solitary, mainly on the exposed area of the body like face and neck. In most cases, the etiology is unknown. However, several triggering factors have been identified including acupuncture, piercings, tattoos, medications, vaccinations, post—herpes zoster scars, insect bites, and *Borrelia burgdorferi* infection.[3] The occurrence of pseudolymphoma and lymphoma in cutaneous lesions of connective tissue diseases (CTD) has rarely been reported. Magro et al[4] reported a series of 17 patients with CTD whose skin biopsies showed atypical lymphoid infiltrates coexistent with features of CTD. Pseudolymphoma was seen in fifteen patients; thirteen patients had lupus, the remaining two patients were found to have relapsing polychondritis and dermatomyositis. Two out of the seventeen patients showed cutaneous T-cell lymphoma; one of whom had been diagnosed with lupus and the other patient with lichen sclerosus/morphea overlap. In our patient, the histological aspect of dense lymphocytic infiltrate with lymphoid follicles associated with clinical nodules, does not correspond to inflammatory morphea or keloid morphea. There was no evidence of Borrelia burgdorferi infection, insect bites, and vaccinations. Atypical lymphoid infiltrates in the cutaneous lesions of CTD generally represent a pseudolymphoma and not a malignant lymphoma.[4] It is conceivable that pseudolymphoma may progress into cutaneous lymphoma; however, it is poorly defined.[5] Therefore, patients should be continually monitored for constitutional signs of lymphoma, and a second biopsy should be done if any unusual clinical change or when the lesions become resistant to conventional treatment modalities, to rule out malignant lymphoma.

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